UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/772,272	02/06/2004	Misa Tominaga	US-108	4146

38108 7590 04/07/2006

CERMAK & KENEALY LLP
ACS LLC
515 EAST BRADDOCK ROAD
SUITE B
ALEXANDRIA, VA 22314

EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 04/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/772,272	TOMINAGA ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *9 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/24/04, 7/30/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is response to Applicant's election of Group I, claims 1-8 with traverse filed on January 10, 2006. Group II, claims 9-10 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

The traversal is on the grounds that the examination of the Groups I and II does not constitute a serious burden. These arguments have been fully considered but are not found to be persuasive for the reasons below:

First, the classification system has no statutory recognition whether inventions are independent and distinct. For example, each class and subclass is comprised of numerous completely independent and distinct patented inventions.

Second, MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed and (2) a serious search and examination burden is placed on the examiner if restriction is not required.

The term "distinct" is defined to mean that two or more subjects as disclosed are related, for example as product and method of use, etc., but are capable of separate manufacture, use or sale as claimed, and are patentable over each other (see MPEP 802.01). In the instant situation, the inventions of Groups I-II are drawn to distinct inventions which are separate products and methods capable of separate manufacture, use or sale as described in the previous Office Action.

Classification of the subject matter is merely one indication of the burdensome nature of the search. The literature search, particularly relevant in this art, is not co-extensive, because for example, Groups I is drawn to products. Groups II is drawn to a method which requires method steps, parameters and endpoints. Clearly different searches and issues are involved in the examination of each Group.

For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a *Bacillus* bacterium which is modified so that growth inhibition by 6-ethoxypurine is reduced and has inosine-producing ability.

The claims broadly encompass a genus of *Bacillus* mutants. There is substantial variability among the species of *Bacillus* mutants encompassed within the scope of the claims. The instant specification teaches that *Bacillus* mutants of the invention can be made by mutagenesis treatment with UV irradiation or treatment with mutagenizing

agent used for typical mutagenesis treatment such as N-methyl-N'-nitro-N-nitrosoguanidine (NTG) and nitrous acid (page 13). The specification teaches that mutations may be made by disruption of the "normal gene" with a "disrupted-type purR gene" (pages 8-9). The instant specification teaches that the disrupted-type purR gene can be obtained by specifically using deletion of a certain region of the purR gene using digestion with restriction enzyme and re-ligation, insertion of another DNA fragment (marker gene etc.) into the purR gene (site-directed mutagenesis). The specification does not place any structure limitations on the *Bacillus* mutants. The instant specification does not teach what locations in the purR gene are mutated to arrive at the claimed *Bacillus* bacterium. The scope of the claims include numerous structural variants and the genus is highly variant because a significant number of structural difference between genus members is permitted. Structural features that could distinguish compounds in the genus from others in the gene class are missing from the disclosure and the claims. No common structural attributes identify the members of the genus. There is no guidance provided as to which nucleic acids can be deleted or substituted and the encode polypeptide still has its biological function. Since the purR nucleic acid sequence encodes a protein, the prior art below teaches the difficulties associated with amino acid modification within a protein.

Thomas E. Creighton, in his book, "Proteins: Structures and Molecular Properties, 1984", (pages 314-315) teaches that variation of the primary structure of a protein can result in an instable molecule. He teaches that a single amino acid change can cause a mutant hemoglobin to have lower stabilities due to any of several causes:

1) alteration of close-packing of the interior; loss of one group that normally participates in a hydrogen bond or salt bridge; 2) the introduction of a charged or polar group into the interior or the insertion into a helical region of a proline residue, which must distort the alpha-helix; 3) while sometimes radical changes of surface groups, even introduction of a non-polar side chain have no great effect on stability.

Thomas E. Creighton, in his book "*Protein Structure: A Practical Approach, 1989; pages 184-186*" teaches that present day site directed mutagenesis of a gene allows any amino acids in a protein sequence to be changed to any other, as well as introducing deletions and insertions". The reference goes on to teach that it is difficult to know which amino acid to change and which is the best residue to substitute for the desired functional and structural effect.

Nosoh, Y. et al in *"Protein Stability and Stabilization through Protein Engineering, 1991" (chapter 7, page 197, second paragraph)* adds support to Thomas E. Creighton, by teaching that results so far accumulated on the stability and stabilization of proteins appear to indicate that the strategy for stabilizing proteins differ from protein to protein and that any generalized mechanisms for protein stability have not yet been presented. The mere recitation of a "...which is deficient in one or more genes negatively acting on the biosynthesis of inosine or involved in degradation of inosine and selected from a purine operon repressor gene, succinyl-AMP synthase gene and purine nucleoside phosphorylase gene" does not provide a structure for the claimed *Bacillus* mutants. One skilled in the art would not recognize from the claimed disclosure that the applicant has taught how to make and use the claimed *Bacillus* mutants. What position within the

purR gene or other genes can be modified to arrive at the claimed bacterium? The specification does not enable numerous *Bacillus* mutants encompassed by the claimed invention. Therefore Applicant have not met the enablement requirements as set forth in U.S.C. 112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-8 are rejected under 35 U.S.C. 102(b) as anticipated by Ishii et al *(Agr. Biol. Chem., Vol. 36, No. 9, p. 1511-1522, 1972).*

Claims 1-8 are drawn to a *Bacillus* bacterium which is modified so that growth inhibition by 6-ethoxypurine is reduced and has inosine –producing ability.

Ishii et al teach *Bacillus subtilis* mutants that have improved inosine production (see the Title and Abstract). Ishii et al teach that the mutants were obtained by methyl-N'-nitro-N-nitrosoguanidine (NG) treatment (page 1512). Claim limitations such as "*Bacillus* bacterium is modified so that growth inhibition by 6-ethoxypurine is reduced" and "...modified so that growth inhibition by 6-ethoxypurine is reduced" are inherent in the teachings of the prior art. Claims limitations such as "wherein the medium has an ethoxypurine content of 2000 mg/L", "wherein the bacterium is cultured by applying a

suspension of the bacterium to a solid medium containing 6-ethoxypurine and a solid medium not containing 6-ethoxypurine, the bacterium shows a relative growth degree of 80 or more which is defined by the following equation: Relative growth degree (%) =[colony diameter (mm) observed in the medium containing 6-ethoxypurine]/[colony diameter (mm) observed in the medium not containing 6-ethoxypurine] x 100", "wherein the solid medium containing 6-ethoxypurine has a 6-ethoxypurine content of 2000 mg/l.", "wherein the solid medium is a minimal medium" and "which is deficient in one or more genes negatively acting on the biosynthesis of inosine or involved in degradation of inosine and selected form a purine operon repressor gene, succinyl-AMP synthase gene and purine nucleoside phosphorylase gene" are being viewed as process limitations. It should be noted that the products of the prior art reference appear to be the same or an obvious or analogous variant of the product claimed by the applicant because they appear to possess the same or similar functional characteristics. The purification or production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art. This is particularly true when properties of the product are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPO 964 (CAFC 1985); In re Marosi, 218 USPO 289, 29222-293 (CAFC 1983); In re Brown, 173 USPO 685 (CCPA 1972). Even if applicant's product can be shown to be of higher purity than the product of the prior art reference, applicant's needs to show some unexpected and unique utility or property, such as unexpected biologically significant increase in specific activity with which the increased purity, greater stability and/or practicality or freedom from some restrictive

element or adverse side effects inherent in the product preparations of the prior art or some other secondary consideration which the additional degree of purity imparts (to which there is a basis in the specification) to applicant's product in order to overcome the aspect of the product's purity is relied upon.

Since the Office does not have the facilities for examining and comparing applicant's bacterium with the bacterium of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the bacterium of the prior art does not possess the same material structural and functional characteristics of the claimed bacterium). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

4. Claims 1-8 are rejected under 35 U.S.C. 102(b) as anticipated by Hitoshi *(European Patent Publication Number 58158197 published September 20, 1983)(Abstract only).*

Claims 1-8 are drawn to a *Bacillus* bacterium which is modified so that growth inhibition by 6-ethoxypurine is reduced and has inosine –producing ability.

Hitoshi teaches *Bacillus subtilis* mutants that have inosine producing ability (see the Abstract). Claim limitations such as "*Bacillus* bacterium is modified so that growth inhibition by 6-ethoxypurine is reduced" and "...modified so that growth inhibition by 6-ethoxypurine is reduced" are inherent in the teachings of the prior art. Claims limitations such as "wherein the medium has an ethoxypurine content of 2000 mg/L",

"wherein the bacterium is cultured by applying a suspension of the bacterium to a solid medium containing 6-ethoxypurine and a solid medium not containing 6-ethoxypurine, the bacterium shows a relative growth degree of 80 or more which is defined by the following equation: Relative growth degree (%) =[colony diameter (mm) observed in the medium containing 6-ethoxypurine]/[colony diameter (mm) observed in the medium not containing 6-ethoxypurine] x 100", "wherein the solid medium containing 6-ethoxypurine has a 6-ethoxypurine content of 2000 mg/l.", "wherein the solid medium is a minimal medium" and "which is deficient in one or more genes negatively acting on the biosynthesis of inosine or involved in degradation of inosine and selected form a purine operon repressor gene, succinyl-AMP synthase gene and purine nucleoside phosphorylase gene" are being viewed as process limitations. It should be noted that the products of the prior art reference appear to be the same or an obvious or analogous variant of the product claimed by the applicant because they appear to possess the same or similar functional characteristics. The purification or production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art. This is particularly true when properties of the product are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 29222-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972). Even if applicant's product can be shown to be of higher purity than the product of the prior art reference, applicant's needs to show some unexpected and unique utility or property, such as unexpected biologically significant increase in specific activity with which the increased

purity, greater stability and/or practicality or freedom from some restrictive element or adverse side effects inherent in the product preparations of the prior art or some other secondary consideration which the additional degree of purity imparts (to which there is a basis in the specification) to applicant's product in order to overcome the aspect of the product's purity is relied upon.

Since the Office does not have the facilities for examining and comparing applicant's bacterium with the bacterium of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the bacterium of the prior art does not possess the same material structural and functional characteristics of the claimed bacterium). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

5. Claims 1-8 are rejected under 35 U.S.C. 102(b) as anticipated by Ajinomoto *(Japanese Patent Publication Number J52154595 published December 22, 1977)(Abstract only).*

Claims 1-8 are drawn to a *Bacillus* bacterium which is modified so that growth inhibition by 6-ethoxypurine is reduced and has inosine –producing ability.

Ajinomoto teaches a *Bacillus* bacterium that have inosine producing ability (see the Abstract). Claim limitations such as "*Bacillus* bacterium is modified so that growth inhibition by 6-ethoxypurine is reduced" and "...modified so that growth inhibition by 6-ethoxypurine is reduced" are inherent in the teachings of the prior art. Claims

limitations such as "wherein the medium has an ethoxypurine content of 2000 mg/L", "wherein the bacterium is cultured by applying a suspension of the bacterium to a solid medium containing 6-ethoxypurine and a solid medium not containing 6-ethoxypurine, the bacterium shows a relative growth degree of 80 or more which is defined by the following equation: Relative growth degree (%) =[colony diameter (mm) observed in the medium containing 6-ethoxypurine]/[colony diameter (mm) observed in the medium not containing 6-ethoxypurine] x 100", "wherein the solid medium containing 6-ethoxypurine has a 6-ethoxypurine content of 2000 mg/l.", "wherein the solid medium is a minimal medium" and "which is deficient in one or more genes negatively acting on the biosynthesis of inosine or involved in degradation of inosine and selected form a purine operon repressor gene, succinyl-AMP synthase gene and purine nucleoside phosphorylase gene" are being viewed as process limitations. It should be noted that the products of the prior art reference appear to be the same or an obvious or analogous variant of the product claimed by the applicant because they appear to possess the same or similar functional characteristics. The purification or production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art. This is particularly true when properties of the product are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 29222-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972). Even if applicant's product can be shown to be of higher purity than the product of the prior art reference, applicant's needs to show some unexpected and unique utility or property, such as

unexpected biologically significant increase in specific activity with which the increased purity, greater stability and/or practicality or freedom from some restrictive element or adverse side effects inherent in the product preparations of the prior art or some other secondary consideration which the additional degree of purity imparts (to which there is a basis in the specification) to applicant's product in order to overcome the aspect of the product's purity is relied upon.

Since the Office does not have the facilities for examining and comparing applicant's bacterium with the bacterium of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the bacterium of the prior art does not possess the same material structural and functional characteristics of the claimed bacterium). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Status of Claims

6. No claims are allowed.

Conclusion

7. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vanessa L. Ford
Biotechnology Patent Examiner
March 21, 2006

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINE
TECHNOLOGY CENTER